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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/772,114	01/26/2001	Michael A. Whitney	AURO1120-5	8989

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary	Application No.	Applicant(s)	
	09/772,114	WHITNEY ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *171-192* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *171-192* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 171-192 are rejected under 35 U.S.C. 103(a) as being unpatentable over Forrester et al (Proc. Natl. Acad. Sci. (February 1996) 93:1677-1682) in view of Tsien et al (U.S. Patent 5,741,657) and further in view of Hicks et al (Meth. Enzymol. (1995) 254:263-275).

Forrester teaches a plurality of eukaryotic clonal cells (see abstract), wherein each clonal cell comprises a distinct fusion RNA of a cellular RNA transcript and a B-galactosidase polynucleotide encoding a B-galactosidase, stating "Integration of PT1-

ATG into the intron of an active gene can generate a fusion transcript between lacZ and an endogenous trapped gene" (see page 1677, column 2) and,

Wherein said clonal cells exhibit as much as a 12.4 fold induction in B-galactosidase expression in response to the induction of expression of said target in said clonal cells (See page 1678, table 1) in response to exposure of said clonal cells to a ligand for said target (see page 1677, column 2),

Wherein said clonal cells were selected from a population of cells transfected with the PT1-ATG vector and wherein said vector lacks a promoter to express said B-galactosidase (See page 1677, column 2).

With regard to claim 172 and 181, Forrester further teaches clonal cells under the control of the retinoic acid response element (see page 1678, table 1).

With regard to claims 173-176, 179, 180, 182 and 183, Forrester teaches the use of 24 well plates (a two dimensional array) (see page 1677, column 2). Forrester teaches screening of 3,600 ES (embryonic stem) cell colonies with 202 positive colonies picked and retested in the 24 well plates (see page 1678, column 1).

With regard to claims 177 and 184, Forrester teaches the use of ES cells which are emybryonic stem cells (see page 1677, column 2).

With regard to claims 187 and 190, Forrester teaches a 12.4 fold induction in B-galactosidase expression (See page 1678, table 1).

Forrester does not teach the use of B-lactamase in the place of B-galactosidase as the reporter. Also, it is unclear whether the vector of Forrester is a viral vector.

Tsien teaches the use of B-lactamase in the place of B-galactosidase (see column 3, lines 34-45). Tsien further teaches the limitation of claims 185 and 188 regarding membrane permeant substrates (see claim 10).

Hicks teaches the use of retroviral gene trap vectors (see page 267, page 268, figure 2 and entire reference).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Forrester to substitute the use the B-lactamase enzyme of Tsien for B-galactosidase since Tsien teaches "B-lactamases are nearly optimal enzymes in respect to their almost diffusion controlled catalysis of B-lactam hydrolysis. Upon examination of the other properties of this class of enzymes, it was determined that they were suited to the task of an intracellular reporter enzyme. (see column 3, lines 34-39)." Tsien identifies advantages of the use of B-lactamase which include high efficiency of the enzyme (see column 3, lines 34-35), since the enzymes are nearly optimally diffusion controlled (see column 3, lines 34-35).

It would further have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Forrester to use retroviral vectors as taught by Hicks since Hicks states that relative to ordinary vectors "[R]etrovirus vectors are easier to use, especially for large scale mutagenesis, and the structure of the recombination products is more predictable (see page 267). An ordinary practitioner would have been motivated to modify the method of Forrester in view of Tsien to use retrovirus gene trap vectors since the method of Forrester is a large

scale mutagenesis method screening 3,600 colonies and since Hicks expressly teaches that this would be easier using a retrovirus gene trap vector.

Response to Arguments

4. Applicant's arguments filed February 9, 2004 have been fully considered but they are not persuasive.

Applicant first argues that the new limitation that the cells were selected by FACS overcomes the 103 rejection because this limitation is not taught by the prior art. This argument is not found persuasive because the method of selecting the cells is a process limitation in a product claim. MPEP 2113 notes "The patentability of a product does not depend on its method of production." In fact, the process limitation imposes NO structural constraints on the resultant cells. In the absence of any structural difference, the argued limitation is NOT, in fact, a limitation at all. It does not impose any requirements on the claim. Therefore, the argument that the prior art does not teach this limitation is not relevant because the product is obvious, however it is made. In the prior art, there is a different mode of selection. Applicant's use of a different mode of selection might render a method unobvious, but not a product. For example, an egg is the same whether it is picked from the chicken coop with your hand, with your mouth, or by rolling them down a conveyor belt. The egg is the same egg. Similarly, the cells in the instant application are the same irrespective of the method of selection.

Applicant then argues that certain elements are missing from particular references. However, these elements are found in other references cited in the prior art rejection. So, for example, Forrester and Hicks teach vectors without signal sequences.

See figure 1 of Hicks for an example of a vector which lacks a signal sequence. Tsien teaches the use of the label as discussed above. These arguments represent an attempt to deconstruct the rejection and apply each reference separately as a 102. If Applicant's intent is to point out that no single reference makes the claims obvious, Applicant is correct. It is the combination of references which renders these claims prima facie obvious to one of ordinary skill in the art, and these references motivate formation of the cells claimed by Applicant for the reasons given in the rejection above.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1634